

Role of FNAC in the Diagnosis of Breast Carcinoma, its Correlation with Histopathology and its Prognostic Importance.

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ABSTRACT

Background: Breast carcinoma is the most common malignant tumor and the leading cause of carcinoma death in women. With an annual incidence of approximately 1, 44,000 new cases of breast cancers in India, it has now become the most common female cancer in urban India and the second commonest in the rural Indian women. Nottingham applied histological grading system, and Robinson applied cytological grading system, which are one of the established methodologies to determine the histological and cytological grade of the tumor. By using these prognostic factors from pathological reports, the prognosis of the patient can be estimated individually. **Aim:** To analyze cytological and histological grading and their correlation along with tumor size and lymphnode status in breast carcinomas and its prognostic importance. **Methods:** All patients presenting with palpable breast lesions were subjected to an FNAC procedure after a detailed history, general physical and local examination. After performing fine needle aspiration diagnosis of various breast lesions were made on the basis of morphological and cytological findings and cytological grading for the malignant breast lesions was done. It was followed by excision biopsy, mastectomy, and cytohistological comparison was done to assess the efficiency and accuracy of cytological grading done after fine needle aspiration. **Results:** The most common type found in study was Ductal carcinoma (not otherwise specified) seen in 95.2% cases. The maximum no. of cases i.e. 36 (44.45%) were found in upper outer quadrant. all patients (100%) presented with complaint of lump in the breast. On assessing all 6 features, the maximum number of cases were in grade- II i.e. 48 (59.3%). A significant agreement was seen between cytological and histological grades. **Conclusion:** Assigning a cytological grade of breast carcinoma aspirates can be done with little effort, is reproducible and with rare exceptions depending on sample limitations correlates precisely with the histological grade. The tumor grading can be used as a very good prognostic and predictive marker for breast carcinomas.

Keywords: Breast carcinoma, Cytological grade, histological grade.

INTRODUCTION

Breast carcinoma is the most common malignant tumor and the leading cause of carcinoma death in women. In our country, though the incidence of breast carcinomas is lower than the west yet it is the second most common malignant tumor in females comprising 16 to 21%, the first being carcinoma cervix. Breast cancers are diagnosed at a relatively advanced stage.^[1] Breast cancer is the most common female cancer in the world with an estimated 1.67 million new cancer cases diagnosed in 2012. This represents about 12% of all new cancer cases and 25% of all cancers in women.^[2] While the age adjusted incidence rates of breast cancer in India is lower than the western countries, because of the large

population the burden of breast cancer is high. With an annual incidence of approximately 1, 44,000 new cases of breast cancers in India, it has now become the most common female cancer in urban India and the second commonest in the rural Indian women. Differentiating benign lumps from malignant preoperatively for definite treatment is necessary. Though histopathological diagnoses is a universally accepted confirmatory mode of diagnosis & follow up, fine needle aspiration cytology of breast lumps is an important part of triple assessment (Clinical examination, imaging and FNAC) of palpable breast lumps. Fine needle aspiration is used to obtain a neat accurate preoperative diagnosis, which acts as a prerogative to the surgeons for the plan of management. It is simple, safe, cost effective, minimally invasive rapid and as sensitive as biopsy.^[3] The utility of FNAC in the diagnosis of breast lesions in the female patients who attended the GSVM Medical College & Hospital has been studied. The study also included the cytological and

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histopathological correlation in the diagnosis of breast lesions and also certain prognostic factors like, tumor size, tumor grade, lymph nodal metastasis, angiogenesis. Nottingham applied histological grading system, and Robinson applied cytological grading system, which are one of the established methodologies to determine the histological and cytological grade of the tumor. By using these prognostic factors from pathological reports, the prognosis of the patient can be estimated individually. Histological grade with Nottingham prognostic index is used to plan for an appropriate therapy in individual patients. More aggressive type of tumors is found in young women with breast cancer. Breast cancer is a multifaceted disease having distinct biological subtypes with diverse natural history, presenting a varied spectrum of clinical, pathologic and molecular features with different prognostic and therapeutic implications. Only about one half of patients with early breast cancer are treated and cured by local surgical excision alone. Therefore, it is important to identify the set of patients in whom the disease is destined to recur and which patients are likely to benefit from systemic chemotherapy.

MATERIALS AND METHODS

Place of Study:

Study was done in department of pathology, G.S.V.M. Medical College Kanpur, during 2 years period from July 2016 to August 2018. A prospective study on breast aspirates was conducted on cases in the department of pathology and attending OPD or hospitalized patients in surgery department of L.L.R Hospital, Kanpur between July 2016 and August 2018.

Inclusion criteria

1. Clinically diagnosed breast malignancy in female of all age group.
2. Patients who give written informed consent.

Exclusion criteria

1. Patients with metastatic malignancy of breast.
2. Patients already treated for contralateral breast cancer.
3. Patients not willing to give written consent.

All patients presenting with palpable breast lesions were subjected to an FNAC procedure after a detailed history, general physical and local examination. After performing fine needle aspiration diagnosis of various breast lesions were made on the basis of morphological and cytological findings and cytological grading for the malignant breast lesions was done. It was followed by excision biopsy, mastectomy, and cytohistological comparison was done to assess the efficiency and accuracy of cytological grading done after fine needle aspiration.

After establishing the cytological grade, paraffin blocks made out of the respective lumpectomy/mastectomy breast tissue were sent for determination of histological grade.

RESULTS

Total 450 breast FNAC were done of which 85 cases diagnosed having malignant lesions. 81 amongst 85(95.2%) were ductal carcinoma (NOS).

Table 1: Cytomorphological Distribution of Malignant Breast Lesions

| Type | No. of Cases (N=85) | Percentage (%) |
|---------------------------|---------------------|----------------|
| Ductal carcinoma (NOS) | 81 | 95.2 |
| Malignant Phyllodes tumor | 1 | 1.2 |
| Lobular carcinoma | 1 | 1.2 |
| Mucinous carcinoma | 1 | 1.2 |
| Medullary carcinoma | 1 | 1.2 |
| Total | 85 | 100 |

The most common type found in study was Ductal carcinoma (not otherwise specified) seen in 95.2% cases. Only 81 cases classified as Ductal carcinoma (NOS) were included in this analysis. Breast carcinoma of special types was specially excluded from this study in accordance with published grading recommendations.

Table 2: Age Distribution of Patients with Breast Cancer

| Age group in years | No. of cases (N=81) | Percentage (%) |
|--------------------|---------------------|----------------|
| <30 | 3 | 3.70 |
| 31-40 | 10 | 12.35 |
| 41-50 | 40 | 49.38 |
| 51-60 | 20 | 24.69 |
| 61-70 | 6 | 7.41 |
| >70 | 2 | 2.47 |
| total | 81 | 100 |

The above table shows that peak incidence of breast cancer is in the 5th decade i.e. 40 cases (49.38%). Closely followed by 6th decade in which 20 cases (24.69%) were reported.

Table 3: Anatomic Distribution of Breast Carcinoma

| Quadrant | No. of cases (N=81) | Percentage (%) |
|-------------------------------|---------------------|----------------|
| Upper outer | 36 | 44.45% |
| Upper inner | 04 | 04.94% |
| Lower outer | 12 | 14.81% |
| Lower inner | 06 | 7.41% |
| Central(within 1cm of areola) | 20 | 24.69% |
| Diffuse | 03 | 03.70% |
| Total | 81 | 100% |

The maximum no. of cases i.e. 36 (44.45%) were found in upper outer quadrant. Followed by the central region which demonstrated a frequency of

24.69%.diffuse involvement of breast was noted in 3 cases.

Table 4: Distribution of Cases According To Symptom Profile

| Symptom | No. of cases (N=81) | percentage |
|------------------|---------------------|------------|
| Lump | 81 | 100 |
| Pain | 07 | 8.64 |
| Ulceration | 05 | 6.17 |
| Nipple discharge | 05 | 6.17 |
| Weight loss | 50 | 61.73 |
| Loss of appetite | 45 | 55.56 |

Table 5: Distribution of Patients According To Local Examination

| Examination findings | No. of cases (N=81) | Percentage (%) |
|------------------------|---------------------|----------------|
| Lump | 81 | 100 |
| Ulcer | 05 | 6.17 |
| Nipple retraction | 18 | 22.22 |
| Chest wall fixation | 09 | 11.11 |
| Pseudorange | 06 | 7.41 |
| Lymph node involvement | 30 | 37.03 |

The above table reveals that all patients (100%) presented with complaint of lump in the breast. The

next most common symptoms are weight loss, 50 cases (61.73%) and loss of appetite in 45 cases (55.56%). Pain is present in 7 cases (8.64%). Both incidence of ulceration and nipple discharge were present in 05 cases (6.17%) each.

The presence of lump was the most frequent finding being observed in 100% of the cases examined. This was followed by the presence of lymphadenopathy in 30 cases (37.03%). The next significant finding was nipple retraction which was seen in 18 cases (22.22%).

Table 6: Distribution of Cases according To Cytological Grading (Robinson's cytological grading system)

| Grade | No. of cases (N=81) | Percentage (%) |
|-------|---------------------|----------------|
| I | 15 | 18.5 |
| II | 48 | 59.3 |
| III | 18 | 22.2 |
| TOTAL | 81 | 100 |

On assessing all 6 features, the maximum number of cases were in grade- II i.e. 48 (59.3%). Grade-I accounted for 15 cases (18.5%). Grade- III was seen in only 18 cases (22.2%).

Table 7: Distribution of the Cytological Features In Tumors (Robinson's cytological grading system)

| Criteria | GRADE I (N=15) | | | GRADE II (N=48) | | | GRADE III (N=18) | | |
|-----------------|----------------|---------|---------|-----------------|---------|---------|------------------|---------|---------|
| | Score 1 | Score 2 | Score 3 | Score 1 | Score 2 | Score 3 | Score 1 | Score 2 | Score 3 |
| Dissociation | 11 | 04 | - | - | 33 | 15 | - | - | 18 |
| Cell size | 12 | 03 | - | - | 48 | - | - | - | 18 |
| Cell uniformity | 10 | 05 | - | - | 48 | - | - | 03 | 15 |
| Nucleoli | 11 | 04 | - | - | 30 | 18 | - | 03 | 15 |
| Nuclear margin | 15 | - | - | - | 48 | - | - | 03 | 15 |
| Chromatin | 15 | - | - | - | 48 | - | - | - | 18 |

Grade I Tumors

All the 15 cases of grade I tumor showed smooth nuclear margin (score 1) and vesicular nuclei (score 1). On assessment of the cell size 12 out of 15 cases had cell size 1-2 times that of RBC (score 1), 3 cases had size 3-4 times that of RBC (score 2). Maximum number of cases that is 10 out of 15 showed cells which were monomorphic (score 1). 11 out of 15 cases revealed cells predominantly in clusters (score 1). 11 out of 15 cases revealed indistinct nucleoli (score 1).

Grade II Tumors

All the cases showed cell size 3-4 times of RBC (score 2). All the cases showed cells with moderate variation in shape and size (score 2). All 48 cases demonstrated nuclei with folds or an irregular nuclear margin (score 2). All the 48 cases showed granular chromatin pattern (score 2). 33 out of 48 cases showed a mixture of single cells and clusters (score 2), while the rest 15 cases showed mostly singly lying cells (score 3). 30 cases demonstrated noticeable nucleoli (score 2), while 18 cases had prominent nucleoli (score 3).

Grade III Tumors

In grade III tumors, all the 18 cases showed cells lying mostly in singly (score 3). All the 18 cases showed cell size > 5 times that of RBC. All the 18 cases showed clumped and cleared chromatin pattern (score 3). Maximum number of cases i.e. 15 out of 18 showed cells with marked variation in shape (score 3). 15 cases out of 18 showed prominent nucleoli (score 3). 15 cases showed nuclei with their margins having buds and clefts (score 3).

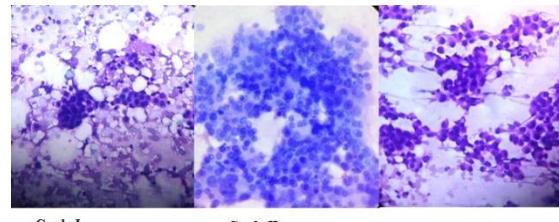


Figure 1: Figure showing cytology of Ductal Carcinoma Cytology of Ductal Carcinoma Brest (H & E 400x)

Table 8: Distribution of cases according to cytological and histological grading

| Cytologic al grading | Histologic al grade I | Histologic al grade II | Histologic al grade III | Total (N=5 0) |
|----------------------|-----------------------|------------------------|-------------------------|---------------|
| | | | | |

| | | | | |
|-----------|----|----|----|----|
| Grade I | 07 | 02 | - | 09 |
| Grade II | 03 | 21 | 03 | 27 |
| Grade III | - | 04 | 10 | 14 |
| Total | 10 | 27 | 13 | 50 |

Out of 81 cases of ductal carcinoma (NOS) diagnosed on cytology, 50 cases were obtained for histopathological examination on follow up. Out of 09 cases of grade-I, 07 cases were grade – I, on histopathology. Out of 27 cases of grade-II on basis of cytology, 21 cases were grade-II on histopathology. 10 out of 14 cases of grade-III on the basis of cytology, were Grade III on Histology while 4 cases were grade-II on histopathology.

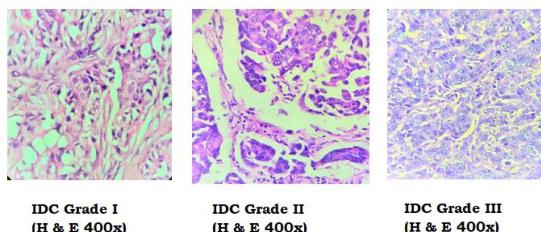


Figure 2: Figure showing Histology of Ductal Carcinoma Cytology of Ductal Carcinoma Brest (H & E 400x)

Table 9: Distribution of Cases according to Tumor Size

| Tumor size (cms.) | No. of cases (n=50) | Percentage |
|-------------------|---------------------|------------|
| <2 | 08 | 16.00% |
| 2-5 | 30 | 60.00% |
| >5 | 12 | 24.00% |

12 cases had tumor size more than 5 cm (T3), 60.00% had tumor size 2 to 5 cm (T2) and 16.00% cases had tumor size between 1 to 2cm (T1).

Table 10: Distribution Of Cases According To Lymph Node Status

| Lymph node status | No. of cases (n=50) | Percentage |
|----------------------|---------------------|------------|
| Not identified | 10 | 20.00% |
| Negative (0) | 07 | 14.00% |
| Positive (1-3) | 18 | 36.00% |
| Positive (4 or more) | 15 | 30.00% |

About 66% cases showed lymph node metastasis

DISCUSSION

Frequency of Malignant Breast Lesions on FNA 95.2% lesions were reported as ductal carcinoma (not otherwise specified), thus forming largest group of this study. Malignant phyllodes, lobular, mucinous and medullary carcinoma were reported in 4.8% of the cases. Similarly Rosen (1979),^[4] stated that invasive duct carcinomas NOS, forms the largest group of malignant mammary tumors constituting 65-80% of mammary carcinomas.

Age Group- In the present study, [Table 2] shows that peak incidence of breast cancer was in age group 41-50 years (49.38%), closely followed by the

age group 51-60 years with incidence of 24.69%. Likewise Okonkwo et al (2008),^[5] in their study stated that maximum number of patients reporting with breast carcinoma are in their 5th decade, with peak incidence being around 45 years. They also stated that majority of the cases in India are seen in the premenopausal age group.

Anatomical Distribution- This study was showed [Table 3] revealed that the breast cancer was most commonly found in upper outer quadrant (44.45%), followed by the central region which demonstrated a frequency of 24.69%. Diffuse involvement was noted in 3.70% of cases. Drabre et al (2005), Akerman et al (1997), Haagensen et al (1971), Ellsworth et al (2004),^[6-9] also reported similar results in his study.

Distribution of patients according to signs, symptoms and local examination All the patients presented with a lump. This was followed by symptoms of weight loss (61.73%), loss of appetite (55.56%). Lymphadenopathy was found in 37.03% cases. Apart from these the other signs and symptoms found were nipple retraction (22.22%), ulceration (6.17%) and pain (8.64%) cases.

Present study that small number of patients presents with the complaint of pain. This is accordance with the study done by Preece et al (1982),^[10] in which he reported that pain is an uncommon presenting symptom of breast carcinoma, seen in only 7% cases. In our study nipple discharge and ulceration were seen in 12.34% of cases. Likewise Haagensen et al (1997),^[8] demonstrated that in breast cancer patients the incidence of nipple discharge and ulceration varied from 10-14% which is in accordance with our study.

Cytological Grading

In the present study cytologic grading was performed on the fine needle aspirations of 81 cases by the Robinson et al (1994),^[11] cytologic grading system. We found 15 cases (18.5%) as grade I, 48 cases (59.3%) grade II, and 18 cases (22.2%) as grade III tumor.

In a similar study done by Khan et al 2009,^[12] on the role of cytological grading in prognostication of breast carcinoma, found out that cytologic grades correlated well with the histologic grades. They also stated that of six parameters studies, cell dissociation, nucleoli and chromatin pattern were the most influential features. Similarly Chhabra et al (2005),^[13] also performed a study with similar results.

Distribution of cases according to cytological and histological grading

In the present study of Table 8, showing the distribution of cases according to cytological and histological grading 50 cases out of 81 were available for histologic grading. The grading was performed and it was found that amongst 09 of cytological grade I tumors 07 (77.78%) were

confirmed as grade I on histology, while 02 was labelled as grade II. 21 (77.78%) of 27 cytological grade II tumors were grade II on histology, and 3 were grade I and 3 were grade III. Out of 14 cytological grade III, 10 (71.4%) proved to be grade III on histology while 4 were redesignated as grade II. A significant agreement was seen between cytological and histological grades. A lack of correlation in 23% cases may be due to tumor heterogeneity and observer subjectivity when assigning a grade. It may be due to the fact that during performing fine needle aspiration, material aspirated may not be true representative of the true grade and pattern of tumor. There are certain limitations with Richardson grading (1957), as it has few criteria to assess nuclear features, as a result of which a slight discrepancy may arise with Robinson cytological grading method (1994).

These results are in accordance with a study done by Sinha et al (2009),^[14] on Robinsons cytological grading in aspirates of breast carcinoma are its correlation with Bloom Richardsons histological grading.

In a similar study done by Pandit and Parekh (2000),^[15] who graded 75 breast carcinomas by Robinsons method and showed 64% concordance with Bloom Richardsons grading. They concluded that cytologic grade could be used to predict the histologic grade as a significant relationship exists between them.

Tumor Size

12 (24%)cases have tumor size>5 cms. 30(60%) cases were having 2-5 cms, and 8 (16%) cases were having less than 2 cms in size. Mushood et al,^[16] study shows that mean size of the lesion was 3.3cm. Majority of our cases (60%) had tumor size of >2 to 5cm. Studies by Suvarchala SB et al,^[17] and Sofi et al,^[18] also recorded majority of patients presenting with tumor size of 2 to 5 cm.

Lymph Node Status

About 66% cases have metastatic lymph node half of them are having >4 metastatic lymph node. In developed countries, in majority of patients lymph node was not involved, but studies carried out in India documented a greater percentage of breast carcinoma with lymph nodal metastasis compared to western figures. In study done by Smriti et al,^[19] cases with lymph node involvement was 74.3%, same were observed by Munjal K et al.^[20] and Moses Ambroise et al.^[21] Most common histological type is invasive ductal carcinoma (NOS) comprises 90% of total cases, which is similar to other Indian studies.

CONCLUSION

FNAC is safe, cost effective and reliable technique for preoperative evaluation of palpable breast lumps. FNAC features are more informative when

combined with physical and radiology features. Grading of malignant lesions on cytology smears must be done for selecting neoadjuvant therapy. Malignant lesions though are more common in fourth and fifth decade, substantial number of cases occurs in third decade. Clinical breast examination and mammography screening should be encouraged in female from the third decade onwards for early detection of breast carcinoma. Assigning a cytological grade of breast carcinoma aspirates can be done with little effort, is reproducible and with rare exceptions depending on sample limitations correlates precisely with the histological grade. The tumor grading can be used as a very good prognostic and predictive marker for breast carcinomas.

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